REMARKS

The Present Invention and Pending Claims

Claims 1, 3, and 13-24 are pending and are directed to a stable lyophilized composition consisting essentially of a PQQ-dependent glucose dehydrogenase, an acid stabilizer selected from a specific group, an albumin, a buffer, and a calcium ion or salt (claims 1 and 13-18), as well as a method of preparing the composition (claims 3 and 19-24). The present invention demonstrates for the first time a PQQ-dependent glucose dehydrogenase-stabilizing effect in a lyophilized composition.

Amendments to the Claims

The claims have been amended to point out more particularly and claim more distinctly the present invention. Specifically, claims 1 and 3 have been amended to replace "comprising" with "consisting essentially of," to remove "aspartic acid" and "glutamic acid" from the Markush group of compounds in section (i), to remove the recitation of "wherein the PQQ-dependent glucose dehydrogenase content is 100 to 2000 kU per gram of the composition," and to recite that the composition comprises a buffer and a calcium ion or a calcium salt. The amendments to claims 1 and 3 are supported by the specification at, for example, page 6, lines 4-16, and page 10, lines 2-17. Claims 13-24 are new, and are supported by the specification at, for example, page 3, line 20, through page 4, line 2, page 6, lines 4-16, and page 10, lines 2-17. Claims 2 and 4-12 have been canceled. Accordingly, no new matter has been added by way of these amendments.

Summary of the Office Action

The Office has rejected claims 8 and 12 under 35 U.S.C. § 112, first paragraph, for alleged lack of enablement. The Office also has rejected claims 1-12 under 35 U.S.C. § 103(a) as allegedly obvious over Sode et al. (*Biotechnology Techniques, 11*(8), 577-580 (1997)) in view of Adachi et al. (JP 09-140378). Reconsideration of these rejections is hereby requested.

Discussion of the Written Description Rejection

The Office contends that a deposit of *Acinetobactor calcoaceticus* NCIMB 11517, which is recited in claims 8 and 12, is required because it is not clear if the written description is sufficiently repeatable to avoid the need for such a deposit. Claims 8 and 12 have been canceled. Accordingly, the rejection is believed to be moot.

Discussion of the Obviousness Rejection

The Office has rejected claims 1-12 as allegedly obvious in view of Adachi et al. and Sode et al. Applicants traverse the rejection for the following reasons.

Claims 2 and 4-12 have been canceled. Claims 1 and 3, as amended, are directed to a stable lyophilized composition consisting essentially of a PQQ-dependent glucose dehydrogenase together with (i) at least one compound selected from the group consisting of α-ketoglutaric acid, malic acid, α-ketogluconic acid, α-cyclodextrin and their salts, (ii) an albumin, (iii) a buffer, and (iv) a calcium ion or a calcium salt, as well as a method of preparing the composition.

Adachi et al. teaches that the combination of a calcium ion and specific amino acids results in a high degree of stabilizing effect on PQQ-dependent glucose dehydrogenases (see, e.g., paragraph [0009], an English translation of which was provided in "Attachment B" of the "Response to Office Action" dated August 18, 2003, and paragraph [0010] of Adachi et al.). Adachi et al. teaches that the *specific amino acids* which exert this stabilizing effect of Adachi et al. are glutamic acid, glutamine, and lysine (see, e.g., Abstract, paragraph [0009], paragraph [0031], and claim 1, of Adachi et al.; English translations of paragraphs [0009] and [0031], as well as claim 1, were provided with the "Response to Office Action" dated August 18, 2003). Therefore, Adachi et al. does not teach or suggest an enzyme composition in which α-ketoglutaric acid, malic acid, α-ketogluconic acid, α-cyclodextrin, and/or their salts are used as a stabilizer, as recited in claims 1 and 3. Furthermore, although Adachi et al. teaches that the enzyme composition may be an aqueous or lyophilized composition (see, e.g., paragraph [0014] of Adachi et al.), Adachi et al. does not provide any Examples of, or fully describe in the specification, lyophilized compositions, as required by the pending claims.

The disclosure of Sode et al. does not remedy the deficiencies of Adachi et al. Specifically, Sode et al. does not teach or suggest the addition of α-ketoglutaric acid, malic acid, α-ketogluconic acid, α-cyclodextrin, and/or their salts to an enzyme composition for use as a stabilizer. Rather, Sode et al. only discloses the use of potassium phosphate buffer, fructose, NaCl, saccharose, betain, sorbitol, trehalose, ammonium sulfate, and mannitol (see, e.g., page 578, column 2, second paragraph, and Figure 2 of Sode et al.). Therefore, one of ordinary skill in the art would not arrive at the invention recited in claims 1 and 3, even if motivated to combine the disclosures of Adachi et al. and Sode et al. Accordingly, the obviousness rejection of claims 1 and 3 is improper and should be withdrawn.

Claims 13 and 19 are new and are directed to a stable lyophilized PQQ-dependent glucose dehydrogenase composition consisting essentially of a PQQ-dependent glucose dehydrogenase together with (i) at least one compound selected from the group consisting of aspartic acid, α-ketoglutaric acid, malic acid, α-ketogluconic acid, α-cyclodextrin and their salts, (ii) an albumin, (iii) a buffer, and (iv) a calcium ion or a calcium salt, as well as a method of preparing the composition. Thus, new claims 13 and 19 differ from claims 1 and 3, respectively, by the recitation of aspartic acid. Claims 14-18 and claims 20-24 are dependent on claims 13 and 19, respectively.

Neither Adachi et al. nor Sode et al. teaches or suggests the addition of aspartic acid, α-ketoglutaric acid, malic acid, α-ketogluconic acid, α-cyclodextrin and/or their salts to an enzyme composition for use as a stabilizer, as recited in claims 13 and 14. In particular, Adachi et al. teaches that *only specific amino acids*, namely glutamine, glutamic acid, and lysine, can be used to stabilize an enzyme composition (see, e.g., Abstract, paragraph [0009], paragraph [0031], and claim 1, of Adachi et al.; English translations of paragraphs [0009] and [0031], as well as claim 1, were provided with the "Response to Office Action" dated August 18, 2003). Furthermore, Sode et al. does not teach or suggest the use of any amino acids as stabilizers, let alone aspartic acid. Accordingly, the subject matter of new claims 13-24 is not obvious in view of Adachi et al. and Sode et al. for the same reasons as discussed above for claims 1 and 3, as well as the fact that one of ordinary skill in the art would not have been motivated by those references to use aspartic acid in the enzyme composition. Since neither Adachi et al. or Sode et al. discloses the addition of aspartic acid, α-ketoglutaric acid, malic acid, α-ketogluconic acid, α-cyclodextrin and/or their salts to an enzyme composition, one of ordinary skill in the art would not have arrived at the inventions of claims 13-24 from the combined disclosures of Adachi et al. and Sode et al. As a result, an obviousness rejection of claims 13-24 would not be proper.

Conclusion

The application is considered to be in good and proper form for allowance, and the Examiner is respectfully requested to pass this application to issue. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned attorney.

Respectfully submitted,

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